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OF THE

PATHOLOGICAL SOCIETY

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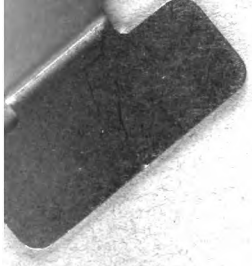

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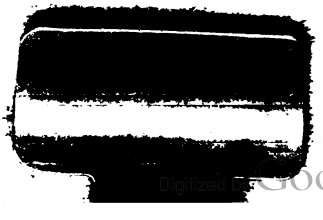

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Proceedings

of the

Pathological Society of Philadelphia.

JULY 1, 1900. NEW SERIES, VOL. III. No. 9.

TABLE OF CONTENTS.

Papillomatous Epithelioma of the Pelvis of the Kidney.

ALOYSIUS O. J. KELLY, M.D.

(*From the Pathologic Institute of the German Hospital of Philadelphia.*)

In consequence of a series of fortuitous circumstances, and also probably because of my interest in the subject, it has been my fortune during recent years to have encountered a considerable number of tumors of the kidney. Among these there have been instances of the more common renal neoplasms, as well as others of greater rarity and interest. They comprise examples of the ordinary tumors of connective tissue origin; of tumors derived from the epithelium of the uriniferous tubules; of others, and the larger number, to be referred to proliferation of aberrant adrenal rests in the kidney; and of still others of complex histology and doubtful genesis. While the study of tumors of the kidney has occupied the attention of this Society on a number of occasions, I have been unable to find in the PROCEEDINGS the record of a single tumor of this organ referred by the reporter to proliferation of aberrant adrenal rests, or of one developed from the pelvis of the

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kidney (or ureter), or of one originating in the kidney capsule. Tumors developing in the kidney capsule and unassociated with aberrant adrenal rests, as well as those arising in the pelvis of the kidney, are of comparative infrequence. On the other hand, new-growths of the kidney that originate from misplaced adrenal rests comprise a relatively large proportion of all tumors of this organ. They have, however, been variously interpreted, and have generally been loosely described as sarcomas, carcinomas, adenomas, endotheliomas, and peritheliomas, with the implied, if not always expressed, conviction of the author, that they were derived from the proper structures of the kidney—the renal epithelium, on the one hand, and the endothelium, or the so-called perithelium, on the other. Since 1883, however, when Grawitz first directed attention to the fact that certain tumors of the kidney, which prior to that time had been imperfectly understood and variously interpreted, were derived from aberrant adrenal tissue in the kidney, these new-growths have been the subject of renewed and careful study. The original observations of Grawitz have received abundant confirmation at the hands of a number of investigators, of whom it will suffice for the present to mention Ambrosius, Chiari, Horn, Marchand, Lubarsch, Ulrich, Manasse, and Gatti. In this connection I trust I may also, without a charge of supererogation, refer to my own previous communication on the subject (*Ueber Hypernephrome der Niere, Ziegler's Beiträge zur path. Anat. u. zur allg. Path.*, Bd. xxiii., 1898; *Philadelphia Medical Journal*, July 30, August 6, 1898).

In view of the importance of the study and proper interpretation of tumors of the kidney, I thought it well to bring the subject to the attention of the Society. As it is manifestly impossible to cover adequately even a small portion of the field of tumor-formations of the kidney at a single sitting, I have elected to present my tumors seriatim, and this evening I exhibit one of the rarer new-growths—a papillomatous epithelioma of the pelvis of the kidney.

The patient was a woman, aged sixty-one years, who was admitted to the Kensington Hospital for Women, May 17, 1899, under the charge of Dr. Charles P. Noble, who very courteously

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afforded me the opportunity to examine the tumor and to report upon its pathologic features. Dr. Noble[1] has already reported somewhat upon the clinical aspects of the case. The patient had complained of hematuria and three distinct attacks of renal colic during the year prior to observation by Dr. Noble, and had become much emaciated. Her family physician, Dr. Edwards, of Williamstown, N. J., was under the impression that two small calculi had been passed. Catheterization of the ureters revealed that the blood came from the right kidney. At operation it was found that a tumor occupied the upper half of the organ, which was accordingly removed. Convalescence was good, and some months later the patient's health was excellent. Recently I have been informed by Dr. Noble that the patient died about nine months after the operation. No necropsy was obtained. There was no evidence of local recurrence, however, and it was presumed that death had resulted from a cerebral affection.

The following is the result of the examination of the tumor, half of which, with the adjoining renal tissue, was kindly given me by Dr. Noble:

Macroscopy: Upon inspection with the unaided eye there is detected in the upper half of the kidney a mass, irregularly spheroid in outline and about the size of a walnut. The major portion of it is situated within the renal parenchyma, but it communicates with the pelvis, which in this region has been destroyed and is represented by a fairly deep crater-like excavation. The edges of the latter are irregular and ragged; the base is likewise irregular and reveals a dense aggregation of excrescences of varying size and length. Many of these are quite soft and necrotic, but the larger portion of the tumor is quite hard. On superficial examination the new-growth is seen to be fairly well circumscribed against the surrounding renal tissue, but close inspection reveals that it is possessed of no capsule. On the contrary, it is seen to invade the kidney tissue in an octopus-like fashion. This is evident from a number of minute roundish or ovoid spaces about the periphery of the growth. These are possessed of a smooth lining, and are filled with prolongations of the tumor. With a fine forceps the latter may be withdrawn a short distance from the

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spaces within which they are situated, thus revealing the absence of intimate association with the surrounding renal tissue. They may not be removed entirely, however, without tearing them, thus revealing their connection with the remaining or main portion of the growth. Many of these prolongations reach to within 4 mm. of the free edge of the cortex of the kidney.

Microscopy: Upon microscopic examination the tumor is seen to be composed of a dense aggregation of papillary excrescences, which course in various directions and invade the renal parenchyma. They vary somewhat in size, and, although they invade the kidney tissue, they are always sharply demarcated against the latter, and they preserve their connection with others of their kind. Each excrescence is composed of a connective-tissue stalk surmounted by a mantle of epithelial cells. The stalk is made up of loose areolar connective tissue, with relatively few cells. In the center of many of them there can be recognized a small capillary vessel. In some of them cells are more conspicuous; others reveal round-cell infiltration, necrosis, and granular débris. The mantles consist of cells, fifteen, twenty, or more layers in thickness. The individual cells are distinctly epithelial in type, and are of moderate size. They are generally cylindric in shape, though a few of the superficial layers evince some tendency to become more cuboid or squamous. Typical squamous cells, however, are not to be detected. The cells have clear vesicular nuclei that stain well, and each usually reveals a single distinct nucleolus. In some regions of the growth the typical appearances are not very distinct; the epithelial cells no longer form distinct mantles, but they tend rather to infiltrate the renal tissue without definite arrangement. The more superficial excrescences reveal considerable necrosis. The kidney itself presents the lesions of a high grade interstitial nephritis, with considerable hyperplastic connective tissue, round-cell infiltration, obliteration of many glomeruli, atrophy of the renal tubules, thickening of the blood-vessels, and compression of the kidney tissue in the neighborhood of the invading new-growth.

From the foregoing description it is therefore evident that the tumor is correctly described as a papillomatous epithelioma,

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originating from the mucous membrane of the pelvis of the kidney.

If one may judge from the scarcity of reported cases, the class of tumors of the kidney, of which the foregoing is an instructive example, belongs among the rarest of renal new-growths. It is difficult, however, to ascertain just how rare these tumors are. By some systematic writers on diseases of the genito-urinary tract they are incidentally referred to; by others they are entirely overlooked. Those who do note their occurrence mention them very briefly, and reference to specific cases is most unusual. When the literature is searched for recorded cases but very few can be found. Thus Ziegler[2] states: "Tumors of the renal pelvis and ureter are rare. There occur, however, carcinomas as well as connective tissue tumors, in part in the form of papillary proliferation. Carcinoma also may ensue upon a calculous pyelitis." Birch-Hirschfeld,[3] in discussing papillomas and carcinomas, does not mention that they may arise from the kidney pelvis. Sutton[4] states that "villous growths, in every way identical with those found in the bladder, are sometimes found growing from the pelvis of the kidney," and that "villous tumors of the renal pelvis appear to be very rare, judging from the paucity of recorded cases." Senn[5] states that "the urinary tract is very often the seat of papilloma, and no part of it is exempt." Morris[6] states that "villous papilloma occurs in the pelvis of the kidney as it does in the urinary bladder, and in a case met with in the post-mortem room of the Middlesex Hospital there were villous growths in the kidney and bladder of the same person." This is probably the case reported by Murchison, of which mention will be made later. Weichselbaum[7] states that carcinoma which in rare cases arises in the renal pelvis or calyces and then invades the kidney itself develops from the so-called transitional epithelium of the implicated mucous membrane, and that under certain circumstances it may assume the characteristic of a squamous epithelioma. Reginald Harrison[8] states: "The pelvic group (of renal tumors) include hydro- and pyonephrosis, . . . villous tumor, and carcinoma. The pelvic mucous membrane has the same structure as the lining membrane of the bladder, and it is, therefore, as we should expect,

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subject to the same varieties of new-growth. Villous tumor is uncommon, but may attain a considerable size. It is exactly like that which grows in the bladder. Squamous-celled epithelioma is the usual kind of carcinoma met with in this locality; it is more frequent than the preceding. Colloid carcinoma is the only other variety. It is very rare." Fuller[9] mentions merely that instances of papilloma of the pelvis of the kidney have been recorded. Bangs and Hardaway[10] state that "papilloma of the pelvis of the kidney presents the characters of papilloma of the bladder, and, indeed, they may coexist." They also refer to Murchison's case. Stengel[11] does not mention this variety of tumor, either in his description of papilloma or of the tumors of the renal pelvis. He does state, however, that primary carcinoma of the renal pelvis is extremely rare. No mention whatever is made of this variety of tumor of the kidney by Orth,[12] Perls,[13] Thoma,[14] Senator,[15] White and Martin,[16] Warren,[17] or Lydston.[18]

When we come to search the literature for reports of specific examples of this class of tumor but very few can be found. I have been able to discover references to but twenty-one such cases. My search of the literature, however, has not been as exhaustive as it might be, and doubtless some reports have escaped my attention. Of the twenty-one tumors, two certainly did not arise in the pelvis of the kidney, and it may well be doubted if several of the remaining did. It seems, therefore, that these new-growths are very rare. They are generally described as villous disease or papilloma of the pelvis of the kidney. In some few instances the tumor has been removed from the kidney, but recurrence has subsequently taken place, and the tumor has thus assumed malignant characteristics. In some cases the tumor has been spoken of as a carcinoma or epithelioma, and it is because of the manifest malignant characteristics of the growth that I present this evening that I choose the latter designation.

The following is a brief synopsis of the reports of cases that I have been able to read in the original:

Murchison[19] reports the case of a man, sixty-five years old, who for two or three years complained of increased frequency in micturition, and later of hematuria, which gradually increased in frequency and amount. Death resulted

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from uremia, which was due to obstruction of both ureters by blood clots derived from tumor growths in the pelves of both kidneys. At the necropsy it was found that the bladder wall about each ureteral orifice was studded with numerous long, delicate, villous processes, which nowhere formed a distinct tumor. The pelves of both kidneys were considerably dilated, and revealed numerous long, villous processes projecting from its surface. These were one to several lines in length. Examination revealed that they were composed of an external layer of epithelium, which enclosed a capillary vessel filled with blood. This is the case which, as already intimated, is referred to by Morris, and by Bangs and Hardaway. It is also mentioned and illustrated by Sutton, who states in this connection: "It is not improbable, from what we know of the habits of warts generally, that in this exceptional instance the vesical warts were due to transplantation of epithelium from the pelvis of the kidney to the mucous membrane of the bladder." Senn, commenting upon this statement, writes: "While this mode of origin is possible, it is more likely that the tumors developed from so many tumor-matrices independently of each other."

Roberts and DeMorgan[20] report the case of a woman, aged seventy years, who for two years presented albuminuria and repeated attacks of hematuria, the latter at times of extreme severity. She then developed bronchitis, and later a strangulated hernia, for the relief of which operation was undertaken. She died, however, five hours later. At necropsy the right kidney was found disorganized, engorged with blood, and so friable as to break with the slightest pressure. The cortex was firm, but the entire pelvis was much dilated and filled with a quantity of débris. This, when removed, revealed a soft, whitish-yellow mass, the size of a damson, occupying the pelvis, from the wall of which it sprang. Examination revealed it to be a villous tumor growing from the lower third of the wall of the pelvis, and attached to it by a thin broad pedicle. A number of other villous growths were found springing from different portions of the wall of the pelvis. They were found to consist of a delicate fibrous stroma surrounded by epithelium.

Gaucher[21] reports the case of a man, aged fifty years, who had been ill for a long time. His principal manifestations had been abdominal pain, vomiting, diarrhea and constipation, emaciation, and an abdominal tumor. There was neither hematuria nor derangement of micturition. He eventually died of erysipelas. The necropsy revealed an encephaloid carcinoma of the kidney and peritoneum, which is reported to have manifestly taken its departure from the pelvis of the kidney. But no sufficient and trustworthy evidence is adduced in support of this assertion, and its correctness may well be doubted.

Israel[22] reports the case of a woman, aged forty-seven years, who had been treated in the gynecologic clinic for cystitis, and who had died with the manifestations of peritonitis. At the necropsy, in addition to the peritonitis, there was found a hydronephrosis of the left kidney, which resulted from the obstruction of the ureter by a large calculus. There was also found a villous growth in the pelvis of the kidney. Microscopically it resembled a medullary carcin-

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oma, revealing an alveolar structure, with variations in the relative amount of stroma and cells in different regions. Israel suggests the possibility of the calculus being responsible for the development of the carcinoma.

Billroth[23] reports the case of a man, aged thirty-three years, who had always enjoyed good health until shortly before he came under observation with the clinical manifestations of an abdominal tumor. At operation a tumor of the kidney, the size of three fists, was successfully removed, and the patient made a good recovery. Billroth observes that the tumor was evidently an interstitial papilloma, originating in the Malpighian capsules and glomeruli. Neuman[24] comments upon this growth, which he regards as a unique example of papilloma of the kidney. Although thus described by Billroth, it is doubtful if this designation would meet the requirements of modern pathology. It is much more likely, despite the designation papilloma, that the neoplasm was an adenoma—a papillary adenoma. Certainly it did not originate from the pelvis, the point of departure of all correctly designated papillomas.

Hartmann[25] reports the case of a man, aged fifty-four years, who was operated upon for calculous pyelitis and obstruction of the ureter. Death resulted. Examination of the left kidney revealed a carcinoma springing from the pelvis and implicating the ureter in addition to other structures. A calculus was also found.

Shattock[26] is reported to have presented, at a meeting of the Pathological Society of London, March 6 (1888 ?), a specimen of true epithelioma of the pelvis of the kidney in association with a calculus. The opinion is expressed that the calculus was the cause of the epithelioma. The reference is in the *Deutsche medicinische Wochenschrift*, but I have been unable to find any mention of the report in the *Transactions of the Pathological Society of London*.

Thornton[27] reports the case of a woman, aged thirty-two years, upon whom nephrectomy was performed for hydronephrosis. This was found to have resulted from a single papillomatous growth and a calculus. The papilloma was the size of a pea, and both it and the calculus were situated at the pelvic end of the ureter. He observes: "From the way in which the stone was hollowed out and capped the papilloma, it seems probable that the growth was the primary disease; from its position it interfered with escape of the urine and produced hydronephrosis, the obstruction to the outflow of the urine leading to a deposit of its salts on the rough surface of the papilloma and the gradual formation of the calculus, which then more effectually blocked the ureter."

Jones[28] reports the case of a man, aged fifty-five years, who for eighteen months was troubled with almost constant throbbing pain in the right loin, hematuria, progressive emaciation (loss of thirty-four and a half pounds), and anemia. At operation a soft villous growth was found occupying the pelvis of the right kidney. This was the size of a thumb, sessile, and much resembled similar growths of the bladder. It was removed by means of a Volkmann's spoon. The small surface remaining was smooth, clean, but vascular. A

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thermocautery was applied to a few bleeding points. Further examination revealed what seemed to be a similar growth higher up in the pelvis, but further operative treatment was abandoned on account of the precarious condition of the patient. Eleven weeks after the operation the general health of the patient had improved. Subsequently pains recurred in the region of the kidney, and at the end of nine months the entire organ was removed. Of the subsequent history of the patient I have been unable to learn anything. This tumor is figured in Kelynack's treatise on renal growths.

Kelynack[29] also mentions another tumor of this class, and writes: "In a specimen of carcinoma of the pelvis of the kidney sent me by Mr. Paul there was an abundant fibroid stroma, with aggregations of large epithelial cells in masses, columns, and small alveolar-like groupings, but presenting no distinct papillomatous structure."

Kundrat,[30] at a meeting of the Gesellschaft der Aerzte in Wien, December 4, 1891, presented three cases of epithelioma of the pelvis of the kidney. In the note of the presentation it is stated that the entire communication will be published subsequently, but I have been unable to find it. Billroth,[31] commenting upon the cases, impressed with the uniqueness of the specimens, remarked that the communication brought forward something entirely new.

Battle[32] reports a case of a man, aged fifty-one years, who presented a history of the passage of a large calculus six years prior to observation, and of the passage of smaller ones since that time. In addition, he complained of pain in the region of the kidney and of hematuria. At operation several dark rounded calculi and many smaller calculi, grains of sand, were removed. In addition, a soft villous tumor was found in the lower portion of the pelvis. The growth was removed, and the site of its attachment was thoroughly scraped with a sharp spoon. The patient recovered from the operation, but at the end of five months hematuria recurred, and later there developed constant pain in the region of the kidney and several calculi were voided. The patient became emaciated and anemic. The entire kidney was then removed and the patient recovered. The development of the tumor was ascribed to the irritation produced by the calculi.

Drew[33] reports the case of a man, aged fifty-six years, who, three and a half years prior to observation, had an attack of pain resembling renal colic. Subsequently there occurred other attacks, and these had been more frequent during the five months immediately preceding observation. In addition, there developed painful and difficult micturition, hematuria, which sometimes was very profuse. There finally ensued swelling of the abdomen, a demonstrable tumor in the renal region, anemia, and emaciation. Nephrotomy was performed, but at the end of some months, before convalescence had been fully established, death resulted. At the necropsy the left kidney was found much enlarged, and the pelvis and calyces much dilated and covered with a delicate papillomatous growth. Delicate tufts of villous growth, attached by a narrow base, were also found all along the ureter. In the bladder springing from the margin of the

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ureteral orifice there was a large papillomatous growth, the base of which did not appear to infiltrate the bladder wall. Microscopically the tumor was found to be composed of branching villi of extreme delicacy, the terminal branches being rounded or club-shaped. In some of these the epithelial cells were arranged so as to suggest the transitional type of epithelium of the urinary tract.

Drew also refers to another specimen in the Museum of Guy's Hospital, and this specimen is also commented upon by Dickenson (quoted by Jones). In this instance a villous growth sprang from the pelvis of a kidney which was enormously dilated. The dilatation is thought to have resulted from the presence of calculi, one of which still remained in one of the calyces. Drew refers to still another specimen of villous growth of the pelvis of the kidney in association with calculi—a specimen in the University College Museum, London.

Kohlhardt[34] reports the case of a woman, aged sixty-nine years, who was well until her sixty-seventh year, when, following an attack of influenza, she presented hematuria. This persisted and gradually grew worse, and was accompanied by pain in the left side, emaciation, and anemia. At operation the left kidney was removed, and the patient recovered. The pelvis of the kidney was found much dilated, and in its lower half there was detected a tumor the size of an egg. This was composed of numerous villous-like excrescences from 2 to 15 mm. in length. Smaller growths were irregularly distributed over other portions of the mucous membrane of the pelvis and calyces and the upper third of the ureters. Microscopically they revealed the usual appearances of such tumors—a vascularized connective tissue stalk surmounted by a mantle of epithelial cells.

Neelsen reports[35] a most interesting case of a man, aged fifty-seven years, who always enjoyed good health until he was obliged to seek the advice of his physician on account of abdominal pain. The physician detected a small tumor in the right side of the abdomen. A short time later the patient became very ill, went into a condition of collapse, with marked dyspnea, pallid lividity, and frequent pulse. There occurred, however, no demonstrable alteration in the tumor. The urine contained a small amount of bile-pigment, a small amount of albumin, but no blood. The patient recovered somewhat, but after the lapse of eight days he had another attack and died. During this attack, and before death, the tumor was found to have enlarged considerably. The necropsy revealed that the right kidney had two ureters. The superior one was occluded, where it dilated to form the pelvis, by multiple villous growths that did not infiltrate the kidney tissue. This occlusion had resulted in hydronephrosis of one-half of the kidney. The other half did not present any noteworthy deviations from the normal. There was also found a papilloma of the bladder, situated 5 cm. from the ureteral orifice, and there was in addition a hemorrhagic perinephritis. Microscopic examination of the tumor revealed the ordinary appearances characteristic of papilloma of the bladder.

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In addition to the foregoing cases, Kelynack writes that Robin and Windle have reported examples of similar tumors. I have been unable to find the original paper of Windle, and from the reports of Robin[36] I have not been able to satisfy myself that he was dealing with a tumor of the nature of those at present under discussion. Finally, a paper by Pantaloni[37] was promising of great interest, but it was, unfortunately, inaccessible.

When we come to consider these cases collectively, we must eliminate the case of Windle, because of the inaccessibility of the original report, and also the cases of Robin and Billroth, because of the extreme likelihood that their tumors did not arise from the renal pelvis. Including, however, the case of Gaucher, concerning the exact nature of which some doubt may well be expressed, there are eighteen cases of tumor originating from the pelvis of the kidney. Adding to these the case reported to-night, there is a total of nineteen cases. Of these, seven occurred in males, five in females; of the remaining seven the sex is not given. With the exception of one, the patients were of advanced age. Thornton's patient was but 32 years of age; eleven patients were aged 47, 50, 51, 54, 55, 56, 57, 61, 65, 67, and 70 years respectively. The ages of the remaining seven were not stated.

In connection with these tumors there are three features that seem of especial interest. These are: 1. The rarity of new-growths of the renal pelvis. 2. The extent of the involvement of the urinary tract in the event of such tumor-formation. 3. The association with some of these tumors of renal calculi.

As regards the first, tumors of the renal pelvis must be accounted very rare. There is scarcely a mucous membrane in the body that is so seldom the seat of tumor-formation as that of the renal pelvis and the ureter. The reason for this is no more understood than is the causation of tumors in general. The tumors that do arise from the mucous membrane of the renal pelvis are the so-called villous disease and carcinoma. It seems to me that the term papilloma is preferable to that of villous disease, and this despite the objection raised by Virchow and others to the designation papilloma. Histologically, these neoplasms exhibit such appearances as we would expect of tumors originating from epi-

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thelium spoken of as transitional, on account of the rapidity of the alteration from the columnar or cylindric character of the deep layers to the squamous type of the superficial cells.

Tumors of the kidney pelvis, histologically papilloma, seem to exhibit marked malignant tendencies, and they have in consequence been designated malignant papillomas This feature is particularly manifest in the cases reported by Jones and Drew, in which the growth only was removed at the primary operation, but in which recurrence subsequently took place, necessitating a secondary operation for the excision of the kidney. The justifiable inference seems to be that, in the event of such tumor being detected at operation, the entire kidney should be removed forthwith, providing, of course, the condition of the other kidney warrants such procedure. The wisdom of such course is evident from the results obtained by operation in the cases reported by Noble and Kohlhardt. In both cases, as already stated, the kidney was removed and the patients recovered.

The second particularly interesting feature in connection with the study of these tumors is the extent of the mucous membrane of the urinary tract involved in some of the cases. In three cases (Noble, Roberts and DeMorgan, Jones) the right kidney was involved; in one case (Israel) the left kidney; in two cases (Hartmann, Kohlhardt) the left kidney and the ureter; in one case (Neelsen) the right kidney and the bladder; in one case (Drew) the left kidney, the ureter, and the bladder; in one case (Murchison) both kidneys and the bladder. In the remaining ten cases it is not ascertainable which kidney was implicated, but it seems probable that the disease did not spread beyond the kidney. In several cases—as, for instance, those of Roberts and DeMorgan, and Jones—in addition to the larger growth, numerous smaller villous excrescences were found attached to other portions of the renal pelvis and calyces. Several reasons have been suggested to explain this multiple involvement, which is quite different from the ordinary metastasis of tumors, and different also from their usual manner of extension by continuity or contiguity of structure. Sutton ascribes it to transplantation of epithelium from the parent growth. Senn, on the contrary, thinks it more likely that the

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different growths originate from as many tumor-matrices. The question cannot be considered definitely settled, though the view of Sutton, which is generally concurred in, is most probably correct. The multiplicity of the lesions in some of these cases may be taken as an argument in favor of the infectious or parasitic nature of tumors, and the likelihood of this receives additional support from the occurrence of certain other diseases of the urinary tract, as ureteritis cystica, due, as is well known, to certain forms of sporozoa.

Finally, and probably the most interesting feature in connection with these new-growths, is the association with some of them of renal calculi. They were found in seven of the cases herewith referred to. In addition, there was a history of several attacks of severe pain resembling renal colic in Drew's case, and a history of the passage of several calculi in the case operated upon by Dr. Noble. The association of renal calculi and tumors of the kidney pelvis is especially interesting from the point of view of cause and effect. It has generally been held that the calculus has operated as the causative factor in the production of the tumor, and this is most probably true. The calculus may mechanically alter the tissues and give rise to the growth, or it may so affect them as to permit of the ready operation of parasites or other cause of tumor-formations. Thornton believes that in his case the tumor was the cause of the calculus, and such were the conditions found that this supposition may be correct. Drew considers the association of calculi with some of these papillomas sufficient to justify him in dividing them into two classes: 1. Diffuse papillomas; and, 2, papillomas with calculi. We must bear in mind that the absence of calculi from some of the cases may be explained upon the assumption that the calculus was originally present and induced the tumor formation, and that it subsequently became disintegrated and was voided with the urine.

This association of tumors of the kidney pelvis and calculi is especially interesting in view of the similar association of biliary calculi with carcinomas of the gall-bladder. The conditions seem quite analogous in the two instances.

In conclusion, and in connection with these tumors, it is inter-

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esting to observe that Kelynack states that Rundle has reported a remarkable case of epithelioma of the ureter in a man, aged forty-six years. I have not been able to find the original paper. I have, however, found the report of another case, that of Jona,[38] who records a case of epithelioma of the left ureter, found accidentally in a subject dead of pneumonitis. The tumor was the size of a hazel-nut, and was situated near the entrance of the ureter into the bladder. The latter author, in his report, refers to the communications of Ribbert, Willutsky, Moser, Thornton, Lebert, Neelsen, Litten, and Hartmann.

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May 24, 1900.

The Rapid Diagnosis of Rabies. (A Preliminary Report.)

M. P. RAVENEL, M.D.,

AND

D. J. McCARTHY, M.D.

Before taking up the newer methods of diagnosis of rabies as suggested by Babes, and later by Van Gehuchten and Nelis, it would be well to review the events which led up to the development of these methods. The work of Balzer, calling attention to the changes in the central nervous system, and especially to the vascular changes, was followed in 1874 by Benedikt's article, in which he described a perivascular infiltration of leukocytes and erythrocytes. Kolesnikoff, in 1876, called attention to an invasion of the pericellular spaces by "indifferent" round cells affecting the hemispheres, cerebellum, and spinal cord, intervertebral and sympathetic ganglia. Schaffer likewise made a very careful study of the vascular and cellular changes, and called attention to "hyaline and fibrillar degeneration and vacuolation of the anterior horn cells of the cord." Nothing of practical importance resulted from these studies until Babes, in 1892, published the results of his investigations. He confirmed the work of his predecessors in this field, described in detail the changes in the ganglion cells of the gray matter, and especially of the bulbar nuclei, and added what he considered to be typical and characteristic lesions of this disease. They were pericellular accumulations of embryonal cells, to which he gave the name "tubercles rabiques." The cells, while presenting various grades of chromatolysis, become surrounded with "embryonal cells," which finally take the place of the destroyed cell.

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He therefore believes that the microscopic examination of the cord furnishes us with the best means for the rapid diagnosis of rabies. Outside of Babes' own laboratory but little use was made of this method. Nelis, working with Van Gehuchten, discovered in the spinal ganglia of two men dead of rabies, and in many of the lower animals, peculiar changes. Normally the intervertebral ganglion is composed of a network of supporting tissue, holding in its meshes the nerve cells, each of which is enclosed in an endothelial capsule. In the rabid animal an infiltration of leukocytes takes place in the stroma, and a proliferation of the endothelial cells of the capsules takes the place of the degenerating cell. These changes are wide-spread and constant. There are but few unaffected capsules, and in advanced cases the section has very much the appearance of an alveolar sarcoma. Van Gehuchten and Nelis question the value of Babes' findings. They consider his cellular changes as secondary, and the nodules rabiques as inconstant and of little value for diagnostic purposes. With a view of determining what of value there might be in these different methods, and to what practical use they might be put in our daily laboratory work, we have examined the cord, medulla, and intervertebral ganglia of the cases coming under our observation. In this, a preliminary report, six cases are detailed. By the fall meeting of this Society we hope to be able to report more fully and with control experiments on this interesting subject.

Of the six cases studied, two were dogs, the others rabbits. The medulla was hardened in formalin, then changed to 96 per cent. alcohol, absolute alcohol, and cut without embedding. (Celloidin embedding was also used in some cases.)

The changes noted in the intervertebral ganglia in all the cases were constant, and corresponded to those described by Nelis and Van Gehuchten. Chromatolytic changes were present in all the cells when stained by the Nissl method, but the capsular changes were best seen in the hematoxylin-eosin sections. And, inasmuch as these latter changes are the essential diagnostic features of the sections, we would suggest that material unfit for the Nissl method would still present the capsular changes when stained by the hematoxylin and eosin. The ganglia of the rabbits presented the most advanced changes. The rabies in these animals was experi-

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mentally produced by means of subdural injections. In all three dogs distinct diagnostic changes had taken place in the cells and their capsules. The changes in the cells are as follows: A diffuse chromatolysis affecting all the cells first takes place. This is followed by a retraction of the cells from the capsule and a proliferation of the cells of the capsule. These newly-formed cells press on the degenerating ganglion cell, and its complete destruction is followed by the filling up of the capsule by the new cells. This stage was only occasionally met with in the dog's ganglion, there being usually a diffuse chromatolysis with proliferation of the capsular cells; not, however, to a sufficient extent to fill up the capsule and obliterate all trace of the ganglion cell.

We have examined the medulla in all the cases for the rabies tubercles of Babes. They were present in five cases, but the method is not so easily carried out and the lesions not so apparent on rapid examination as in the method described by Nelis.

June 14, 1900.

Report of a Case of Malignant Endocarditis Treated with Antistreptococcic Serum.

JAMES HENDRIE LLOYD, M.D.,

AND

ALICE M. SEABROOK, M.D.,

H. A. L., white, female, aged thirty-two years, physician; family history negative; she was not a strong child, and suffered much from follicular tonsillitis; had malaria when about fourteen; had measles and whooping-cough. In January, 1897, she was much exposed during damp, cold weather. She was in charge of a dispensary in Baltimore, and had a great deal of out-door practice. She had an attack of inflammatory rheumatism, involving in succession nearly all the joints, especially marked in the knees, ankles, and wrists. At this time she suffered greatly with the pain in the teeth, and was unable to lie down for days. She was not under any special medical care, and lacked the proper attention. The attack

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was complicated by endocarditis. She discovered this herself by hearing the murmur with the "pillow as a sounding-board."

February 20, 1897, she was admitted to the Methodist Hospital in this city. At this time she had a temperature of 102° to 103.5° F. Pulse 120 to 140.

There was some dyspnea and very profuse sweats of acid reaction. Cough was very troublesome at times. On examination the apex beat was found to be slightly displaced, and auscultation revealed a loud blowing murmur in left heart, transmitted to the axilla and back. The urine showed a small amount of albumin and a few casts.

Treatment was attended by steady improvement, and on April 1st she began duty again as resident physician, doing substitute work in the hospital, though still remaining under treatment.

July 1, 1897, she took charge of the Englewood (N. J.) Hospital, and was actively engaged in work from that time until the date of the last attack.

During the late summer and early fall of 1899 she began to lose ground. Previous to this she had been able to walk several miles without inconvenience, and had also learned to ride a bicycle. Early in October she was obliged to give up and stay in bed several days. During this time she had some daily rise of temperature, not accurately recorded, and a number of rose-colored spots appeared on the chest and abdomen. She thought she was going to have typhoid fever, but in a few days the spots disappeared and the temperature dropped to normal. For several months there had been a troublesome cough; this increased.

On November 21, 1899, she was again admitted to the Methodist Hospital. The temperature on admission was 101.2° F. The urine showed a small amount of albumin and a few hyaline and granular casts. There was marked tenderness over the abdomen, and slight enlargement of the spleen. The old heart murmur was still there.

On December 3d some rose-colored spots appeared over the chest and abdomen, and the blood gave the Widal reaction; the diazo reaction could not be obtained. From this time on the disease ran an even course as a mild type of typhoid fever.

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On December 8th there was a severe attack of epistaxis. The blood would not clot, and both nostrils had to be packed. This occurred a number of times at intervals varying from a few hours to several days. Constipation was persistent.

During December and the first week in January there was little variation in the case. The temperature rarely rose above 103° and never dropped below 99.2° F. until January 9th, when it dropped slowly, reaching normal on the 10th. It rose almost immediately, and did not again fall to so low a point. The epistaxis again showing itself, Dr. Fetterolf was called in and made an examination of the nose and throat. He found the right nostril almost occluded in the posterior portion, and a tendency to bleed whenever touched.

The heart symptoms were increased about this time; at times she could not sleep on account of the throbbing. There were some dyspnea and a sense of oppression over the heart. The murmur was very marked.

After January 18th the temperature became much more irregular, the diurnal variations being more marked.

Cough occurred at times. Precordial pain not a marked symptom, but present at intervals. There was great prostration, occasional chills, followed by profuse sweats, and the mental condition was at times not quite clear.

January 30th, Dr. J. C. Wilson was called in consultation. He concurred in a diagnosis of malignant endocarditis, and he recommended the use of the antistreptococcic serum. Ten c.c. of this were given January 31st. It produced no appreciable change in the temperature or pulse, but brought out a plentiful crop of urticaria. This was most marked on the side of the body in which the injection was given.

February 2d, 10 c.c. more were given, with much the same result. The immediate effect was to make the patient very nervous.

February 5th, 10 c.c. were again given, with the first effects more marked. In this instance there was a marked cellulitis in the surrounding tissues. The injection was made in the right side of breast just below the clavicle. The shoulder and arm were swollen and painful. She was unable to move her arm, and could not bear to

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have the shoulder touched. In a few minutes after the injection of the serum the entire body was covered with urticaria. The itching was intense. The temperature was not affected, rising only to 101.8° F., no higher than on the days when no injection was given. The pulse ran up from 100 to 130, and the nervous disturbance was great. The injection was followed by general prostration.

February 7th the temperature ran up to 102.8° F. and the next day reached 103° F. In the afternoon of the 8th 10 c.c. of serum were injected into the right thigh. The eruption following the injection was more marked than at any previous time and was more persistent. The whole right side was affected, swollen, red, and painful. The inguinal glands on that side were enlarged. The physical discomfort and prostration were very marked. Locally the inflammation was relieved somewhat by soothing applications. There was some involvement of the hip-joint in this inflammatory condition, extension of the thigh being very painful.

February 10th, in the afternoon 20 c.c. of serum were injected into the right breast near the point where the first injection was made. The distress and pain following this was greater than at any previous time, and the temperature ran up to 103.8° F., pulse 142, respiration 24. The pain and discomfort was so great and the exhaustion so marked that it was a question whether any more should be given.

February 15th another injection was made in the right thigh. The symptoms were repeated with added severity, although the injection was only 10 c.c. The exhaustion was very marked and the eruption more annoying than before.

February 17th the temperature dropped from 103.6° to 98°, and the next day came down to 96.8° F., the patient being completely prostrated.

February 22d, 10 c.c. were again injected in the right breast. The temperature rose after the injection to 104°, then dropped again to subnormal. The prostration was so great that it was decided not to give another dose of the serum.

February 23 there was some bowel disturbance. Mucus was present in the stool, and there was a great deal of straining; no blood was present.

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On March 6th the patient passed a large quantity of pus unmixed with feces.

Rectal examination was made by Dr. Norris, who diagnosticated a retroperitoneal abscess which had ruptured into the large intestine.

On March 9th the nasal septum became perforated.

About March 15th the patient became entirely hemiplegic on the right side, the effect doubtless of an embolus from the heart.

On March 20th internal strabismus was noted.

Death occurred on March 27, 1900.

REPORT OF AUTOPSY. *Abdomen:* Omentum extends into pelvis. Colon "M" shaped. Appendix bound down to cecum. *Heart:* There was an anemic infarct near the apex on the left side. The mitral valve was seat of extensive vegetative endocarditis. Weight of heart, 14 ounces; markedly enlarged; pericardial sac contains little or no fluid. Right lung has a few recent adhesions anterior and posterior. Weight, 20 ounces. Left lung has many adhesions posteriorly and to the diaphragm. Both lobes markedly congested, hypostatic, dark; both lobes bound together. Weight, 17 ounces. *Liver:* Distinctly enlarged, capsule adherent to the diaphragm. Weight, 3 pounds 7 ounces. *Spleen:* Much enlarged. Weight, 15 ounces. There were three infarcts: one red in color, the others white. *Kidneys:* Right, very soft, a little enlarged. Weight, 6½ ounces. Capsule strips easily. Very pale and fatty. Left kidney about the same. Cortex of each much diminished. *Intestine:* An area of marked thickening and congestion was found just at the beginning of the sigmoid flexure, and a similar one was found in the cecum. No abscess was found, but evidence of marked catarrh of the colon. *June* 14, 1900.

Rupture of an Aortic Leaflet in a Case of Right Hemiplegia with Aphasia Due to Cerebral Hemorrhage.

AUGUSTUS A. ESHNER, M.D.

C. D., an unmarried laborer, forty-three years old, was admitted to the Philadelphia Hospital on January 31, 1900, complaining of shortness of breath, palpitation of the heart, and severe pain in

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the precordium. He had been a heavy drinker, and admitted syphilitic affection. The action of the heart was rapid and forcible. The apex beat was in the fifth interspace in the mid-axillary line. A loud, high-pitched, rasping murmur was heard over the entire precordium, systolic in time, with greatest intensity at the junction of the second right costal cartilage with the sternum. The urine contained albumin and granular tube-casts. Early in the morning of February 4th the patient was seized with complete right hemiplegia and aphasia, from which he gradually, though not wholly, recovered. On May 3d he died suddenly, after having complained of pain in the lower part of the chest and spitting blood. Postmortem examination, made by Dr. R. C. Rosenberger, disclosed croupous pneumonia of the right lung, pericarditis, pleurisy with adhesion, healed tuberculosis of the left lung, red atrophy of the liver, with beginning cirrhosis, mitral and aortic endocarditis, edema, and softening of the brain. The heart weighed 440 grams. The mitral leaflets were the seat of slight thickening and contraction. Two of the cusps of the aortic valve exhibited well-marked fenestration, while the middle cusp, unfenestrated, was completely torn from its attachments on one side. The aorta was the seat of beginning but well-marked atheroma. Both hemispheres of the brain were edematous, and the left contained a large area of hemorrhagic softening in the situation of the basal ganglia. The kidneys were enlarged and congested.

This case presents two points of especial interest, namely, the rupture of the aortic leaflet and the occurrence of right hemiplegia and aphasia from cerebral hemorrhage in the presence of valvular disease of the heart. The hemorrhage was the earlier lesion, and death must be attributed to the rupture of the valve-leaflet from causes residing within the circulatory mechanism. It was a natural supposition during life to attribute the paralysis and the speech disorder to softening due to obstruction of a branch of the left middle cerebral artery by a plug detached from aortic vegetations. The differentiation of cerebral hemorrhage, embolism, and thrombosis is confessedly difficult, but confidence in diagnostic ability in this connection must be greatly shaken when it is realized that, as in this case, hemorrhage may occur under the exact conditions that would ordinarily be expected to give rise to embolism,

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namely, the existence of disease at the aortic valve and the development of right hemiplegia and aphasia. Perhaps the absence of convulsions should have suggested freedom of the cortex from softening in consequence of interference with its blood-supply.

May 24, 1900.

Peculiar Fluid Obtained From a Malignant Tumor of the Breast by Tapping.

DAVID RIESMAN, M.D.

The fluid was obtained from the largest tumor of the breast that I have ever seen. The unfortunate possessor is a colored woman, a widow, fifty years of age, a cook by occupation. The tumor began as a small lump in the right breast about nine months ago, and grew rapidly without causing any pain until the patient had an attack of bronchitis in March, when the breast hurt her on coughing.

When she was able to leave her bed I had her see a surgeon, who declared the tumor inoperable. The breast then was almost thrice the size of the other mamma, and there was an enlarged gland, the size of an egg, at the anterior right axillary fold.

As the tumor grew it became very heavy, and had to be supported by bandages; it also rendered it difficult for the patient to turn herself from side to side. The skin, which was never broken, gradually became very tense, and fluctuation was obtainable. At this time the increase in size was visible almost from day to day. Thus on May 30th the breast had a circumference of 82½ cm., and on June 2d, three days later, of 89 cm. On this day I tapped the tumor and withdrew 3 pints of a reddish-brown bloody fluid. At the second tapping, on June 14th, I withdrew again 3 pints of fluid, and to-day I obtained without difficulty about 7½ pints.

The fluid, which has been the same on all three tappings, is bloody in character, flows easily, is not spontaneously coagulable, and in color resembles Worcestershire sauce. It decomposes readily, but is sterile, inoculation of culture-media having given negative results. It has a specific gravity of 1020, is neutral in

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reaction, and becomes solidly coagulated on boiling. Microscopically it shows some red blood-corpuscles and isolated small round cells with refractive granules. There is, however, very little sediment, and microscopic examination of it does not afford any clue as to the histologic nature of the tumor, *i. e.*, whether it is a sarcoma or a carcinoma.

There is no evidence of metastasis to internal organs, the nipple is not retracted, the skin not adherent; the tumor, however, appears closely attached to the chest.

The origin of the fluid is explicable on the theory that a large hemorrhage occurred into the tissues of the tumor with the formation of a sanguineous cyst or cysts. The red corpuscles are apparently rapidly dissolved.

A blood examination made a month ago gave the following results: red corpuscles, 4,960,000; white corpuscles, 12,000; hemoglobin, 50 per cent. A striking feature was the marked fibrin production—the fibrin quickly formed a dense network in the native preparation. The patient's anemia at the present time is most profound, and apparently steadily increasing.

June 28, 1900.

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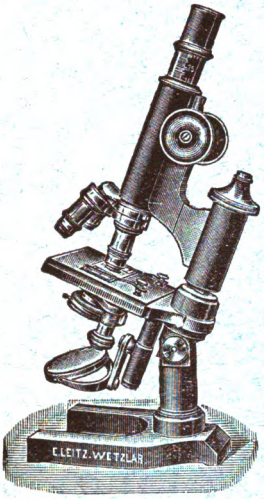

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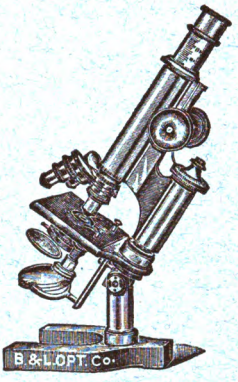

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